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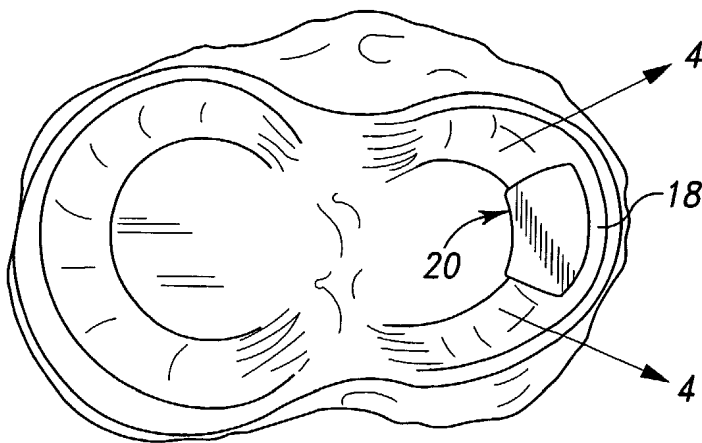
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(54) Title: CARTILAGE REPAIR AND REGENERATION DEVICE AND METHOD



(57) Abstract: A method for the repair of a cartilaginous tissue defect, a cartilage repair device (20) and a method of making a cartilage repair device are disclosed. In the method for the repair of a cartilaginous tissue defect, a device comprising a scaffold, for example an extracellular matrix material, is implanted into the defect, and a biological lubricant (234) is administered to the defect. The device (20) comprises a scaffold (100), for example a naturally occurring extracellular matrix material, and a biological lubricant (234).



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CARTILAGE REPAIR AND REGENERATION DEVICE AND METHOD

CROSS REFERENCE TO RELATED APPLICATIONS

Cross reference is made to co-pending U.S. patent applications Serial
5 No. XX/XXX,XXX entitled "Meniscus Regeneration Device and Method" (Attorney
Docket No. 265280-71141, DEP-745); Serial No. XX/XXX,XXX entitled "Devices
from Naturally Occurring Biologically Derived Materials" (Attorney Docket No.
265280-71142, DEP-748); Serial No. XX/XXX,XXX entitled "Cartilage Repair
Apparatus and Method" (Attorney Docket No. 265280-71143, DEP-749); Serial No.
10 XX/XXX,XXX entitled "Unitary Surgical Device and Method" (Attorney Docket No.
DEP-750); Serial No. XX/XXX,XXX entitled "Hybrid Biologic/Synthetic Porous
Extracellular Matrix Scaffolds" (Attorney Docket No. 265280-71144, DEP-751);
Serial No. XX/XXX,XXX entitled "Porous Extracellular Matrix Scaffold and
Method" (Attorney Docket No. 265280-71146, DEP-747); Serial No. XX/XXX,XXX
15 entitled "Cartilage Repair and Regeneration Scaffolds and Method" (Attorney Docket
No. 265280-71180, DEP-763); and Serial No. XX/XXX,XXX entitled "Porous
Delivery Scaffold and Method" (Attorney Docket No. 265280-71207, DEP-762),
each of which is assigned to the same assignee as the present application, each of
which is filed concurrently herewith, and each of which is hereby incorporated by
20 reference. Cross reference is also made to U.S. Patent Application Serial No.
10/172,347 entitled "Hybrid Biologic-Synthetic Bioabsorbable Scaffolds" which was
filed on June 14, 2002, which is assigned to the same assignee as the present
application, and which is hereby incorporated by reference.

25 BACKGROUND OF THE INVENTION

Articular cartilage is a type of hyaline cartilage that lines the surfaces
of the opposing bones in a diarthrodial joint (e.g., knee, hip, shoulder, etc.). Articular
cartilage provides a near-frictionless articulation between the bones, while also
functioning to absorb and transmit the compressive and shear forces encountered in
30 the joint. Further, since the tissue associated with articular cartilage is aneural, these
load absorbing and transmitting functions occur in a painless fashion in a healthy
joint.

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Fibrocartilage is found in diarthrodial joints, symphyseal joints, intervertebral discs, articular discs, as inclusions in certain tendons that wrap around a pulley, and at insertion sites of ligaments and tendons into bone. Made of a mixture of collagen type I and type II fibers, fibrocartilage can also be damaged, causing pain in the affected joint. It is understood for purposes of this application that the term “cartilage” includes articular cartilage and fibrocartilage.

When cartilage tissue is no longer healthy it can cause debilitating pain in the joint. For example, articular cartilage health can be affected by disease, aging, or trauma, all of which primarily involve a breakdown of the matrix consisting of a dense network of proteoglycan aggregates, collagen fibers, and other smaller matrix proteins. Tissue cells are unable to induce an adequate healing response because they are unable to migrate, being enclosed in lacunae surrounded by a dense matrix. Further, since the tissue is avascular, initiation of healing by circulating cells is limited. Similarly, damage or degeneration of knee fibrocartilage i.e., the menisci, is a common occurrence. A damaged or degenerated meniscus has little ability to heal or repair itself because the pathology frequently occurs in the avascular part of the tissue.

Several articular cartilage repair strategies have been attempted in the past. These include surgical techniques such as microfracturing or performing abrasion arthroplasty on the bone bed to gain vascular access, and hence, stimulate extrinsic repair in the defective region. The long-term outcome of these techniques, however, has been known to result in mechanically inferior fibrocartilagenous tissue.

Another surgical technique is mosaicplasty or osteochondral autograft transfer system (OATS). In this case, cylindrical plugs of healthy articular cartilage from a low-load bearing region of the knee are taken and transplanted into the defective region. This technique, however, can result in excessive donor-site morbidity and associated pain. Additionally, surgeons have reported that the gaps between the round transplants are frequently filled with fibrocartilage which can eventually erode away, thus potentially compromising the integrity of repair throughout the affected area.

The only FDA-approved cartilage treatment product in the market involves autologous chondrocyte implantation (CartiCel™). Autologous chondrocyte implantation involves performing an initial biopsy of healthy cartilage from the

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patient, isolating the cells from the tissue, expanding the cells *in vitro* by passaging them in culture, and then reintroducing the cells into the defective area. The cells are retained within the defect by applying a periosteal tissue patch over the defect, suturing the edges of the patch to the host tissue, and then sealing with fibrin glue.

5 The efficacy of this expensive procedure, however, has recently been put into question by studies that have shown that only a few of the injected cells are retained within the defect and that they may not significantly contribute to the repair process. The healing observed is similar to that observed with microfracture or abrasion of the bone bed, suggesting that it is the preparation of the bone bed and not the introduction
10 of the cells that facilitates the healing process.

Tissue engineering strategies for healing cartilage are being investigated by several academic and commercial teams and show some promise. One approach primarily involves using a carrier or a scaffold to deliver cells or stimulants to the defect site. The scaffold material can be a purified biologic polymer
15 in the form of a porous scaffold or a gel (purified collagens, glycoproteins, proteoglycans, polysaccharides, or the like in various combinations) or porous scaffolds of synthetic biodegradable polymers (PLA, PGA, PDS, PCL, or the like, in various combinations). Several challenges remain with this approach, however. Some of these challenges include retention of the active stimulant at the defect site,
20 inability to control the rate of release of the stimulant (resulting in tissue necrosis due to overdose), and cytotoxicity of the cells due to the degradation by-products of the synthetic polymers.

In another technique, various collagen scaffolds have been used to provide a scaffold for repair and regeneration of damaged cartilage tissue. U.S.
25 Patent No. 6,042,610 to ReGen Biologics, hereby incorporated by reference, discloses the use of a device to regenerate meniscal fibrocartilage. The disclosed device comprises a bioabsorbable material made at least in part from purified collagen and glycosaminoglycans (GAG). Purified collagen and glycosaminoglycans are co-lyophilized to create a foam and then cross-linked to form the device. The device can
30 be used to provide augmentation for a damaged meniscus. Related patents 5,735,903, 5,479,033, 5,306,311, 5,007,934, and 4,880,429 also disclose a meniscal augmentation device for establishing a scaffold adapted for ingrowth of meniscal fibrochondrocyts.

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It is also known to use naturally occurring extracellular matrices (ECMs) to provide a scaffold for tissue repair and regeneration. One such ECM is small intestine submucosa (SIS). SIS has been described as a natural biomaterial used to repair, support, and stabilize a wide variety of anatomical defects and traumatic injuries. See, for example, Cook® Online New Release provided by Cook Biotech at “www.cookgroup.com”. The SIS material is reported to be a naturally occurring collageneous matrix derived from porcine small intestinal submucosa that models the qualities of its host when implanted in human soft tissues. Further, it is taught that the SIS material provides a natural matrix with a three-dimensional structure and biochemical composition that attracts host cells and supports tissue remodeling. SIS products, such as Oasis material and Surgisis material, are commercially available from Cook Biotech, Bloomington, IN.

An SIS product referred to as RESTORE Orthobiologic Implant is available from DePuy Orthopaedics, Inc. in Warsaw, Indiana. The DePuy product is described for use during rotator cuff surgery, and is provided as a resorbable framework that allows the rotator cuff tendon to regenerate itself. The RESTORE Implant is derived from porcine small intestine submucosa that has been cleaned, disinfected, and sterilized. Small intestine submucosa (SIS) has been described as a naturally occurring ECM composed primarily of collagenous proteins. Other biological molecules, such as growth factors, glycosaminoglycans, etc., have also been identified in SIS. See Hodde et al., *Tissue Eng.* 2(3): 209-217 (1996); Voytik-Harbin et al., *J. Cell Biochem.*, 67:478-491 (1997); McPherson and Badylak, *Tissue Eng.*, 4(1): 75-83 (1998); Hodde et al., *Endothelium*, 8(1):11-24 (2001); Hodde and Hiles, *Wounds*, 13(5): 195-201 (2001); Hurst and Bonner, *J. Biomater. Sci. Polym. Ed.*, 12(11) 1267-1279 (2001); Hodde et al., *Biomaterial*, 23(8): 1841-1848 (2002); and Hodde, *Tissue Eng.*, 8(2): 295-308 (2002), all of which are incorporated by reference herein. During seven years of preclinical testing in animals, there were no incidences of infection transmission from the implant to the host, and the RESTORE Implant has not decreased the systemic activity of the immune system. See Allman et al., *Transplant*, 17(11): 1631-1640 (2001); Allman et al., *Tissue Eng.*, 8(1): 53-62 (2002).

While small intestine submucosa is available, other sources of submucosa are known to be effective for tissue remodeling. These sources include,

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platform or plateau and the femur condyles (such indicated at 12). The meniscus serves to reduce contact stresses and wear in the knee joint.

The portion 14 removed from the structure shown in Fig. 1 includes a portion of the original meniscus which was within the avascular zone, particularly the
5 radially inner portion, and may include a portion of the original meniscus which was within the vascular zone.

Fig. 2 shows how an ECM device may illustratively be inserted into the space 16 to be against the outer rim 18. This illustrative device 20 is shown in Figs. 3 and 4 in position filling the space 16 and against the rim 18 left by the
10 surgeon. Fig. 4 shows the device as comprising an upper cover or upper panel 22 and a lower cover or lower panel 24. These panels 22, 24, which may illustratively be angularly related, will define an internal space 26 between the covers. Internal space 26 may be filled with a biological material or a biological structure providing a framework for regeneration of the meniscus into the space 16.

15 Device 20 may be inserted, for example, in arthroscopic surgery through portals provided in the outer anterior surface of the knee opening into the knee cavity between the condyles 12 and the tibial platform 10. However, any surgical procedure to insert a device into damaged cartilage is within the scope of the present invention. As shown, the upper cover 22 of the device 20 will serve as a
20 bearing surface for the condyle 12 disposed thereabove and be subjected to the compression and stress forces involved in articulation of the knee. The condyle will move upon the upper surface of the cover 22. The device 20 will serve as a cushion or pillow for handling the compression load provided by the knee.

Turning to Figs. 5, 6 and 7, it will be seen that an illustrative device is
25 somewhat diagrammatically illustrated. The illustrative device 30 includes an upper panel 32 and a lower panel 34 defining a wedge-shaped device having a base portion 36 and an apex portion 38. Fig. 6 suggests that the device may include a formed wedge-shaped cavity 39 (illustrated in phantom) and that the device may be folded about a fold line 40 to provide a device such as indicated at 42 in Fig. 7. While the
30 Fig. 5 device 30 suggests an open wedge-shaped design, the device 42 in Fig. 7 suggests that, between the upper and lower panels 32, 34 a mass of biological material may be disposed. In Fig. 6, a plurality of tacks 44 are shown attached to one of the

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two panels of the device to be used for securing the device to surrounding tissue in the knee. The panels 32, 34 may be trimmed to the desired wedge shape.

Panels 32, 34 are made from an ECM, illustratively SIS. In one embodiment, a plurality of layers of a naturally occurring ECM such as SIS may be layered together to form panels 32, 34. Optionally, the panels may be toughened, to better withstand the forces within the joint. Copending U.S. Application Serial No. XX/XXX,XXX entitled "Meniscus Regeneration Device and Method" (Attorney Docket No. 265280-71141, DEP-745), already incorporated by reference, teaches methods for toughening the panels. The mass of biological material may comprise, for example, comminuted ECM, fibrin, platelet rich plasma (PRP), blood clot, or some combination thereof.

Referring now to Figs. 8-10, there are shown devices similar to those shown in Figs. 6-7, except that device 100 need not be wedge shaped. Device 100 comprises panels 102 and 104, with a pillow 106 of biological material shaped to fill the void in meniscus 111 left after a partial meniscectomy, as illustrated in Fig. 1. The pillow is placed between panels 102 and 104. In the illustrative embodiment, pillow 106 is smaller than panels 102 and 104, and wing portions 105 of panels 102 and 104 extend beyond pillow 106.

As shown in Fig. 8, device 100 may be provided with barbed darts 112 extending from wings 105. A needle or similar device would be used to push the barbed darts 112 into or through the meniscus to secure device 100 to the meniscus. Barbed darts may be made of any biocompatible material sufficiently rigid to secure device 100 to the meniscus. Barbed darts 112 may be provided integrally with device 100 or may be added by the surgeon prior to insertion of the device.

The device 100 illustrated in Fig. 9 is similar to the device shown in Fig. 8, except that instead of barbed darts, the device of Fig. 9 is provided with sutures 113. The device of Fig. 9 may be affixed to the meniscus in a manner similar to that of the device of Fig. 8. A needle or similar device would be used to push the sutures 113 through the meniscus. As illustrated in Fig. 10, the sutures may be tied together on the outside of the meniscus to form knots 120 that secure device 100 in place.

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While in the various embodiments discussed herein, tacks and sutures have been shown for anchoring the devices, it will be appreciated that the devices may be anchored by any other method at the choice of the surgeon.

Figs. 11 and 12 illustrate several scaffolds that can be used in conjunction with a biological lubricant for cartilage repair. Referring now to Fig. 11, a cartilage repair device 210 is provided for repairing damaged or diseased cartilage. The device 210 includes an anchor 212 which is anchored or otherwise positioned in an opening formed in both a section of native cartilage 216 and the underlying subchondral bone 218. The anchor 212 is configured to be secured in an area from which damaged, diseased, or destroyed native cartilage and possibly bone have been removed. The anchor 212 includes an elongated central body portion 220 and a head portion 222. The body portion 220 extends downwardly from a lower surface of the head portion 222. As shown in Fig. 11, the body portion 220 may have a number of barbs 224 extending therefrom for engaging the sidewalls of the opening formed in the bone 218. In the illustrative embodiment described herein, the barbs 224 extend radially outwardly and are inclined slightly toward the head portion 222 of the anchor 212.

The cartilage repair device 210 also includes a plug 226. The plug 226 is secured to the anchor 212. Specifically, the plug 226 is secured to the upper surface of the head portion 222 of the anchor 212. The plug 226 allows for communication across the removed portion (i.e., the portion of the native cartilage 216 from which the damaged or diseased cartilage has been removed) and the adjacent healthy cartilage. As such, the plug 226 functions as a chondrogenic growth-supporting matrix for promoting a positive cellular response in an effort to achieve articular cartilage regeneration.

The anchor 212 of the cartilage repair device 210 may be constructed of numerous types of synthetic or naturally occurring materials. For example, the anchor 212 may be constructed with a bioabsorbable polymer. Examples of such polymers include: polyesters of [alpha]-hydroxycarboxylic acids, such as poly(L-lactide) (PLLA), polyglycolide (PGA); poly-p-dioxanone (PDS); polycaprolactone (PCL); and any other bioresorbable and biocompatible polymer, co-polymer or mixture of polymers or co-polymers that are commonly used in the construction of prosthetic implants. Moreover, the anchor 212 may be constructed with a naturally

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It is expected that various combinations of bioactive agents, biologically derived agents, cells, biological lubricants, biocompatible inorganic materials, biocompatible polymers can be used with the scaffolds and methods of the present invention.

5 It is expected that standard disinfection and sterilization techniques may be used with the products of the present invention.

EXAMPLE 1

10 A meniscus is prepared as shown in Fig. 1. An SIS device as shown in Fig. 8 is inserted into the space created by the menisectomy and secured by suturing with 5-0 nylon sutures to the surrounding meniscal tissue. The incisions are closed and 2 ml of a solution of 1% sodium hyaluronate, of molecular weight between 2.4 and 3.6 million Daltons (the commercially available ARTHREASE™ high molecular weight sodium hyaluronate) is injected into the knee joint cavity adjacent to the SIS
15 device. After 3 weeks, 95% or more regeneration of the meniscal defect was seen in two out of three dogs. Moreover, the cartilage is mature and is similar in appearance to natural tissue.

 In contrast, use of ARTHREASE™ injections alone, without the SIS implant, resulted in no tissue regeneration within the meniscal defect in three out of
20 three dogs. Use of an SIS implant alone, without ARTHREASE™ injections, resulted in approximately 80% tissue regeneration in one dog and less than 50% regeneration in two of three dogs in this group.

EXAMPLE 2

25 A meniscus is prepared and a device inserted, as in Example 1. The incision is closed and HA (the commercially available ARTHREASE™ high molecular weight sodium hyaluronate of EXAMPLE 1) is injected as in Example 1. Additional injections are provided two weeks and four weeks post-op. It is understood that other protocols for a series of injections may be used.

30

EXAMPLE 3

 A meniscus is prepared as in Example 1. An SIS device as shown in Fig. 8 is placed in an HA solution (the commercially available ARTHREASE™ high

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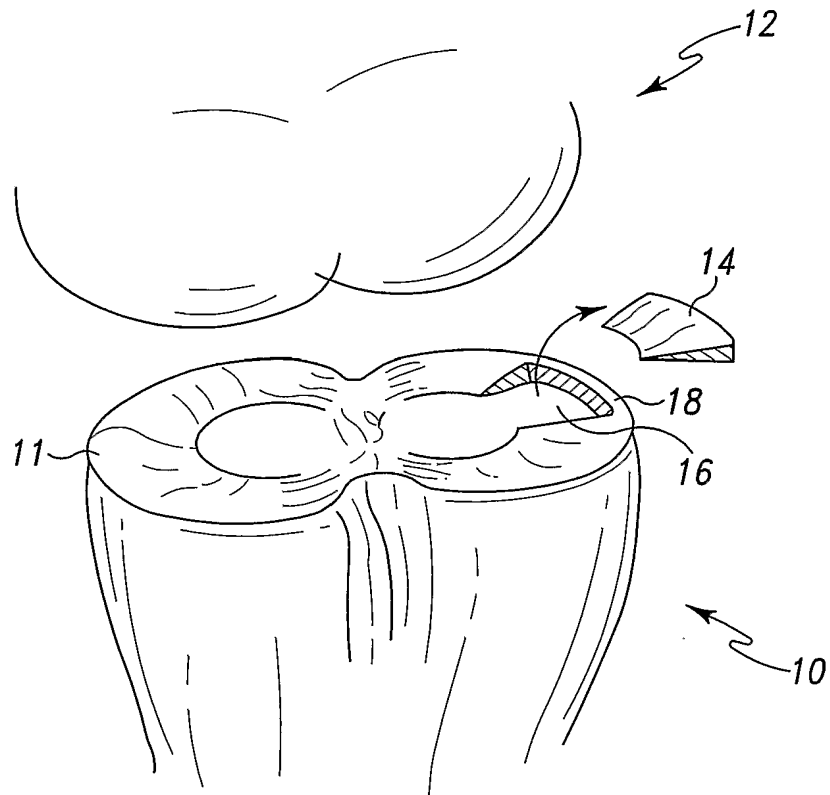


Fig. 1

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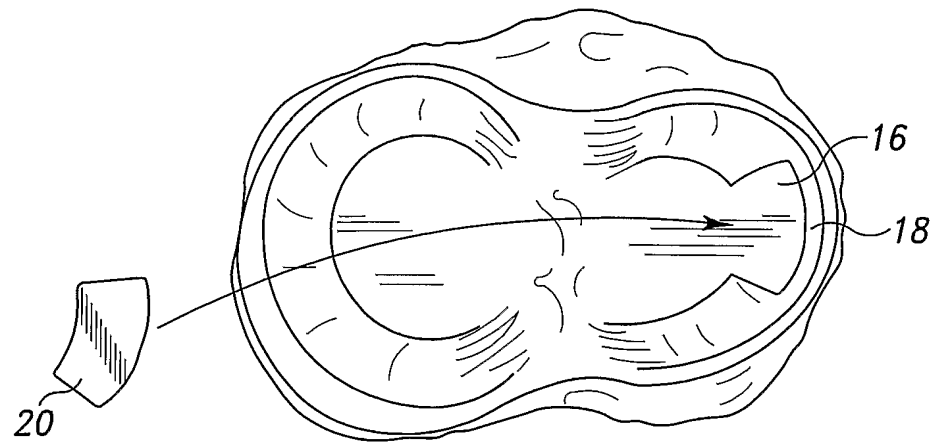


Fig. 2

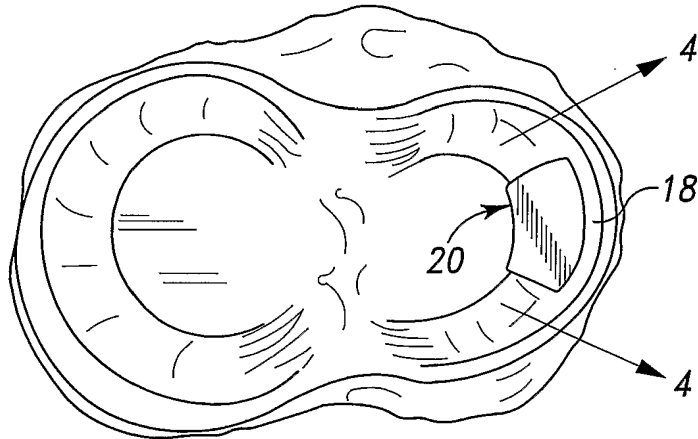


Fig. 3

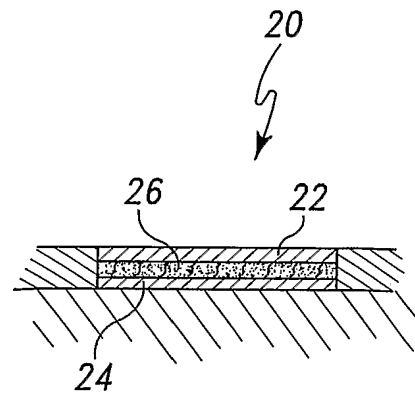


Fig. 4

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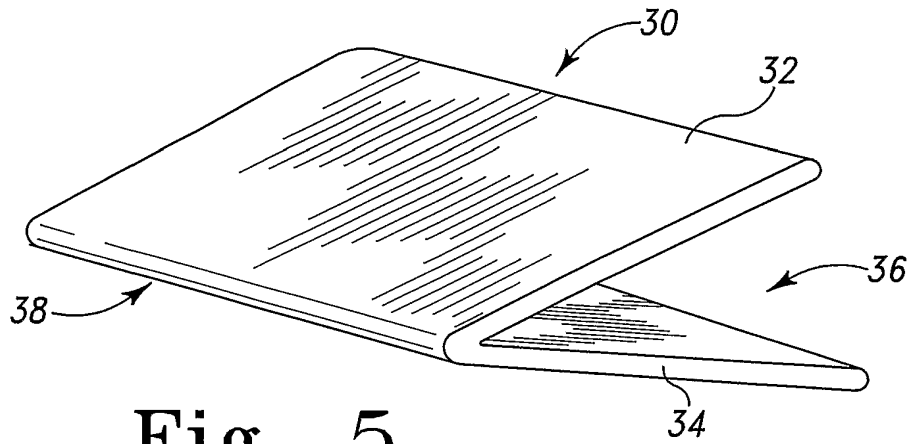


Fig. 5

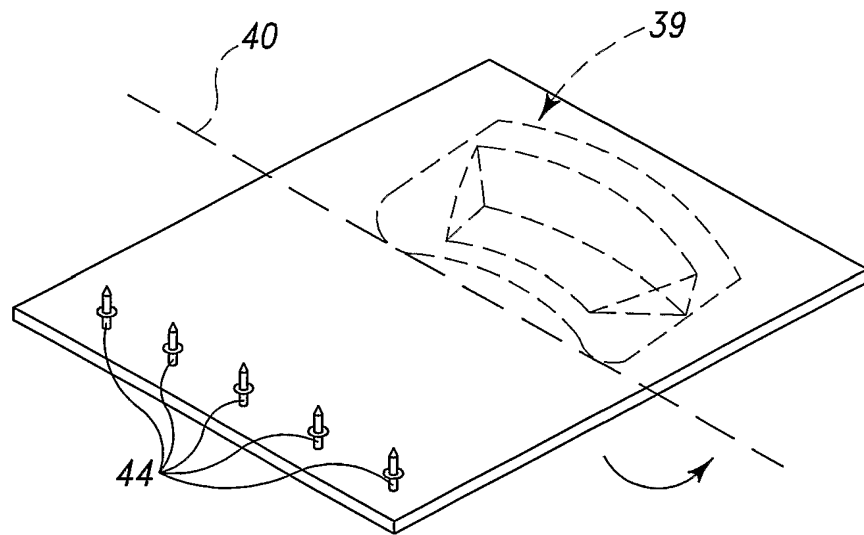


Fig. 6

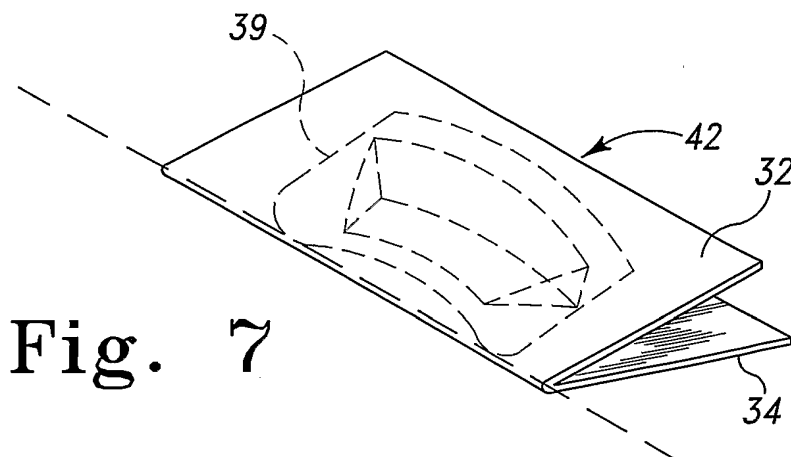


Fig. 7

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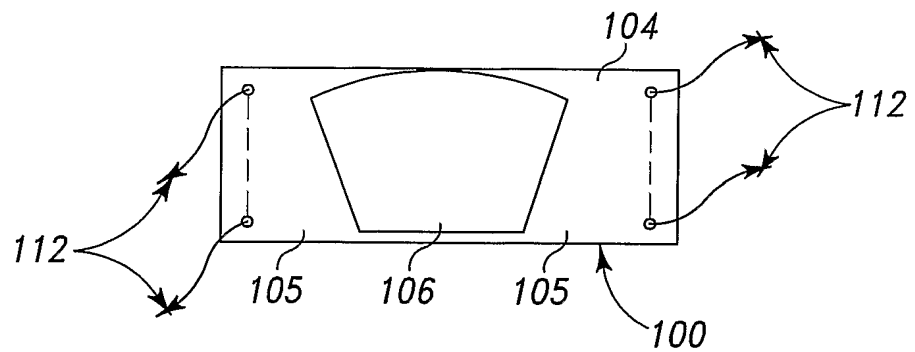


Fig. 8

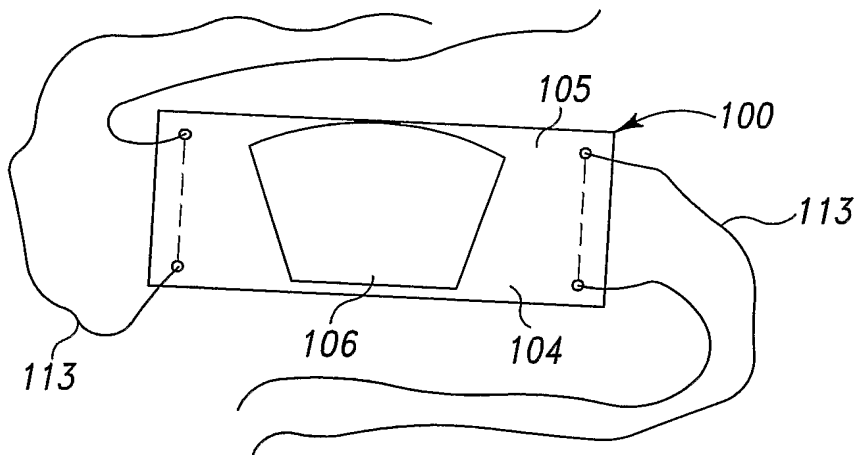


Fig. 9

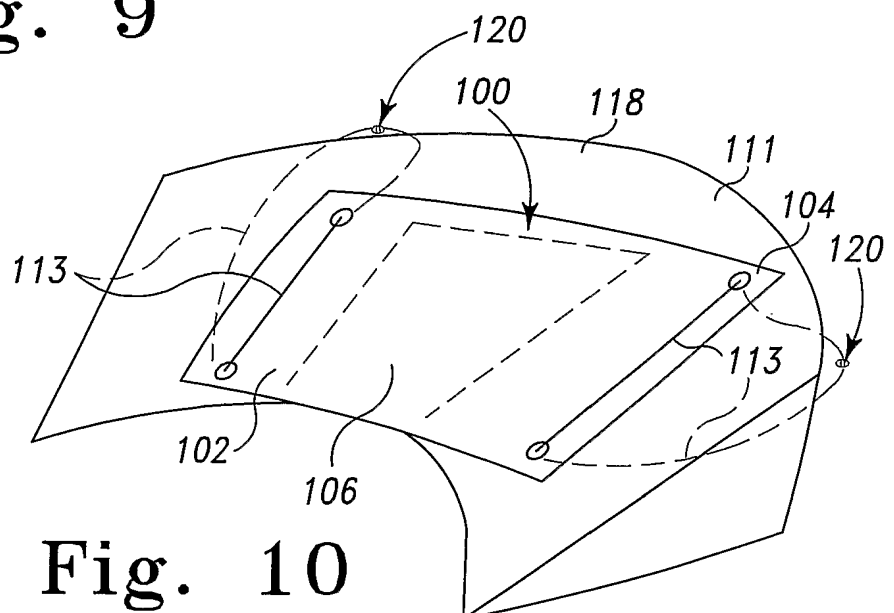


Fig. 10

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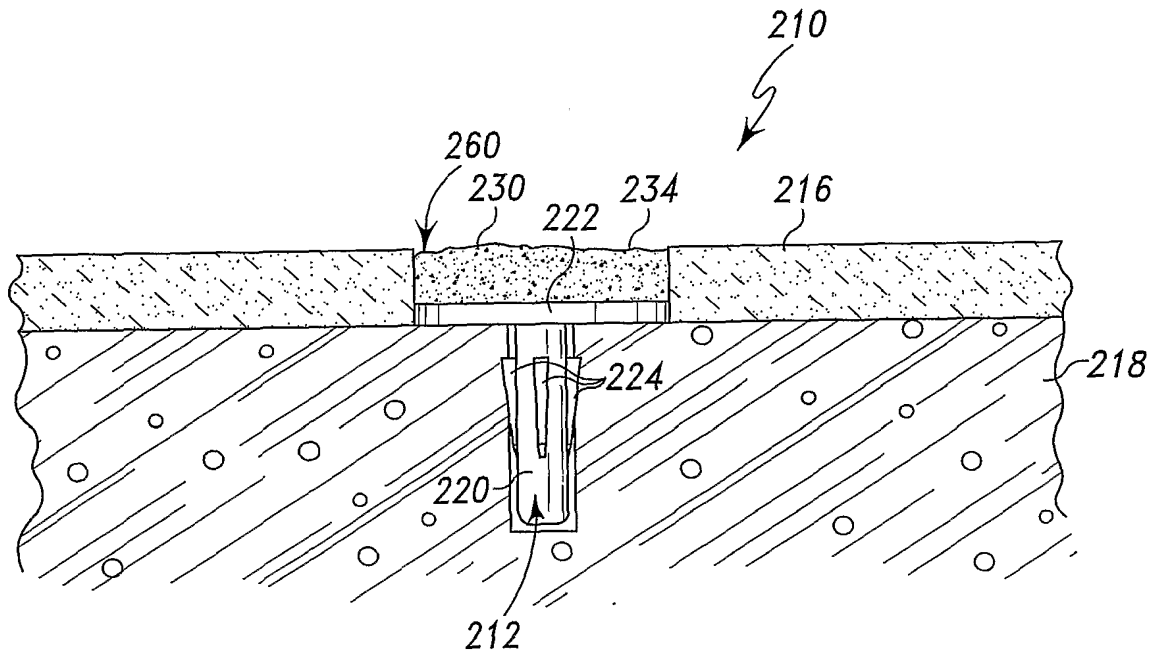


Fig. 11

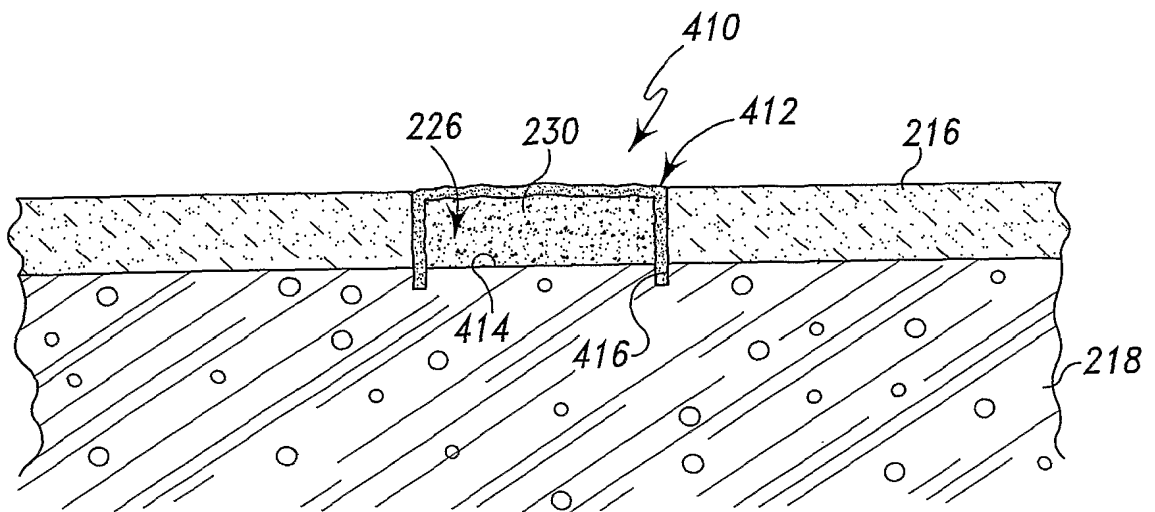


Fig. 12